

# UC- 781



**Drug Class:** Microbicides

## **Drug Description**

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UC-781 is a thiocarboxanilide nonnucleoside reverse transcriptase inhibitor (NNRTI). [1]

## **HIV/AIDS-Related Uses**

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UC-781 is an NNRTI currently being developed as a vaginal microbicide to prevent HIV transmission. UC-781 has been studied in animal models and has entered a Phase I clinical trial in humans.[2] [3]

## **Pharmacology**

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In vitro studies have shown UC-781 to be a rapid, tight-binding inhibitor of HIV-1 reverse transcriptase.[4] It is effective against transmission of both cell-free and cell-associated HIV and has an intracellular antiviral protective effect, with a half-life of 5.5 days.[5] [6]

In vitro exposure of human cervical tissue to 0.5 microM UC-781 for 30 minutes followed by extensive wash of the residual drug resulted in 95% reduction of subsequent viral infection as determined by immunohistochemistry and p24 determination. Furthermore, 1 microM UC-781 pretreatment for 20 minutes, or 10 microM UC-781 pretreatment for 2 minutes, resulted in total protection of the cervical tissue from both T- and M-tropic HIV-1 isolates, as well as from cell-associated HIV-1 infection. Twenty-minute incubation with 10 microM UC-781 completely protected the cervical tissue, even when it was challenged with HIV-1 48 hours after the drug pretreatment. UC-781 was not toxic to the cervical tissue, even when the tissue was exposed to 10 microM UC-781 for 24 hours.[7]

UC-781 has been studied with AZT in vitro. A 1:1 molar combination of AZT plus UC-781 showed high-level synergy in inhibiting replication of an AZT-resistant clinical isolate of HIV. The time to the development of HIV resistance to a 1:1 molar combination of AZT and UC-781 was significantly delayed compared to that for either drug alone.[8]

UC-781 demonstrates a memory effect, in which cells treated in vitro with the drug are protected

from HIV-1 replication for at least 12 days.[9] [10]

A Phase I study of the safety and acceptability of three different doses of UC-781 is underway.[11]

## **Drug and Food Interactions**

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UC-781 exhibits synergy with the NRTI zidovudine in vitro.[12]

## **Clinical Trials**

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For information on clinical trials that involve UC-781, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: UC-781 AND HIV Infections.

## **Dosing Information**

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Mode of Delivery: Intravaginal.[13]

Dosage Form: Topical gel of 0.1%, 0.25%, or 1.0%.[14]

## **Chemistry**

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CAS Name: 3-Furancarbothioamide,

## Chemistry (cont.)

CAS Number: 178870-32-1[16]

Molecular formula: C17-H18-Cl-N-O2-S[17]

C60.8%, H5.4%, Cl10.6%, N4.2%, O9.5%,  
S9.5%[18]

Molecular weight: 335.5[19]

## Other Names

UC781[20]

UC 781[21]

NSC 675186[22]

## Further Reading

Dezzutti CS, James VN, Ramos A, Sullivan ST, Siddig A, Bush TJ, Grohskopf LA, Paxton L, Subbarao S, Hart CE. In vitro comparison of topical microbicides for prevention of human immunodeficiency virus type 1 transmission. Antimicrob Agents Chemother. 2004 Oct;48(10):3834-44. PMID: 15388443

Motakis D, Parniak MA. A tight-binding mode of inhibition is essential for anti-human immunodeficiency virus type 1 virucidal activity of nonnucleoside reverse transcriptase inhibitors. Antimicrob Agents Chemother. 2002 Jun;46(6):1851-6. PMID: 12019100

Van Herrewege Y, Michiels J, Van Roey J, Franssen K, Kestens L, Balzarini J, Lewi P, Vanham G, Janssen P. In vitro evaluation of nonnucleoside reverse transcriptase inhibitors UC-781 and TMC120-R147681 as human immunodeficiency virus microbicides. Antimicrob Agents Chemother. 2004 Jan;48(1):337-9. PMID: 14693562

Van Herrewege Y, Penne L, Vereecken C, Franssen K, van der Groen G, Kestens L, Balzarini J, Vanham G. Activity of reverse transcriptase inhibitors in monocyte-derived dendritic cells: a possible in vitro model for postexposure prophylaxis of sexual HIV transmission. AIDS Res Hum Retroviruses. 2002 Oct 10;18(15):1091-102. PMID: 12396448

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## Further Reading (cont.)

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Zussman A, Lara L, Lara HH, Bentwich Z, Borkow G. Blocking of cell-free and cell-associated HIV-1 transmission through human cervix organ culture with UC781. AIDS. 2003 Mar 28;17(5):653-61. PMID: 12646787

## Manufacturer Information

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UC-781  
Cellegy Pharmaceuticals, Inc  
3490 Oyster Point Boulevard  
Suite 200  
South San Francisco, CA 94080  
(650) 616-2200

## For More Information

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Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: [http://aidsinfo.nih.gov/live\\_help](http://aidsinfo.nih.gov/live_help) Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

## References

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3. Cellegy Pharmaceuticals, Inc - Press Release, 10/8/04; Cellegy Pharmaceuticals to Acquire Biosyn, Inc. Available at: <http://www.cellegy.com/newsroom/press/08oct04.html>. Accessed 12/03/04.
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5. J Virol - 1997 Apr;71(4):3023-30
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8. Antimicrob Agents Chemother - 1999 Feb;43(2):259-63
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